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High rates of death and hospitalization follow bone fracture among hemodialysis patients

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Altered bone structure and function contribute to the high rates of fractures in dialysis patients compared to the general population. Fracture events may increase the risk of subsequent adverse clinical outcomes. Here we assessed the incidence of post-fracture morbidity and mortality in an international cohort of 34,579 in-center hemodialysis patients in the Dialysis Outcomes and Practice Patterns Study (DOPPS). We estimated country-specific rates of fractures requiring a hospital admission and associated length of stay in the hospital. Incidence rates of death and of a composite event of death/rehospitalization were estimated for 1 year after fracture. Overall, 3% of participants experienced a fracture. Fracture incidence varied across countries, from 12 events/1000 patient-years (PY) in Japan to 45/1000 PY in Belgium. In all countries, fracture rates were higher in the hemodialysis group compared to those reported for the general population. Median length of stay ranged from 7 to 37 days in the United States and Japan, respectively. In most countries, postfracture mortality rates exceeded 500/1000 PY and death/rehospitalization rates exceeded 1500/1000 PY. Fracture patients had higher unadjusted rates of death (3.7-fold) and death/rehospitalization (4.0-fold) compared to the overall DOPPS population. Mortality and hospitalization rates were highest in the first month after the fracture and declined thereafter. Thus, the high frequency of fractures and increased adverse outcomes following a fracture pose a significant health burden for dialysis patients. Fracture prevention strategies should be identified and applied broadly in nephrology practices.

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Mineral and endocrine disturbances in the course of chronic kidney disease result in altered bone structure and function, including abnormalities in bone turnover, mineralization, and volume,[1] that likely contribute to the elevated rates of bone fracture observed in the dialysis population as compared with the general population.[2–5] The magnitude of this risk may vary by bone histology types depending on, for instance, the presence of osteomalacia, high-turnover bone disease, or adynamic bone disease.[6,7] In addition, the presence of certain risk factors including abnormal parathyroid hormone (PTH) levels and the use of narcotics and psychoactive medications may increase the likelihood of fracture.[2,3,8]

In the general population, patients experiencing a major bone fracture (for example, hip fracture) have a marked increase in subsequent morbidity and mortality, especially among the elderly.[9–12] In the frail dialysis population, the immediate- and long-term burden for patients who experience a fracture may be substantial, although this has not been thoroughly investigated, particularly in populations outside the United States. One study of dialysis patients in the United States[2,8,13] reported nearly twofold higher mortality rates (1.99) among patients who experienced a hip fracture (774.9/1000 patient-years (PY)) than those who did not (360.2/1000 PY).[13] For dialysis populations outside of the United States, aside from a previous analysis using DOPPS data (1996–2001) describing fracture rates,[3] there are no contemporary data describing fractures or postfracture clinical outcomes.

The aim of this study was to assess health burden related to bone fractures in an international cohort of patients receiving in-center hemodialysis. Using data from the Dialysis Outcomes and Practice Patterns Study (DOPPS), we (1) estimated country-specific rates for all-cause and hip-specific fractures requiring hospitalization; (2) estimated postfracture rates of hospitalization and death, and (3) compared these rates of hospitalization and death after fracture with the rates observed in the overall DOPPS population.

RESULTS

Study sample

A total of 36,337 patients were enrolled over the three DOPPS phases across the 12 participating countries. Of these, 1758

patients had missing or incorrect follow-up data and were excluded, leaving 34,579 patients for the final analysis. A total of 1122 participants (3%) experienced a fracture requiring hospitalization (491 hip fractures, 643 other fractures) during the follow-up period. The overall median length of follow-up was 1.6 years (interquartile range = 0.8–2.4); median follow-up following a fracture requiring hospitalization was 0.6 years (interquartile range = 0.2–1.2). Over the follow-up period, the majority of patients (59%) were administratively censored; 20% died or withdrew from hemodialysis; 8% switched modality; and 12% were transferred to another facility. Table 1 shows patient characteristics for all DOPPS participants included in this analysis, as well as for those who did and did not experience fracture-related hospitalization, stratified by DOPPS region. Patients who experienced a fracture requiring hospitalization during follow-up were older, more likely to be female and white (North America only), had lived for more years on dialysis, had lower body mass index, and higher PTH and Kt/V compared with those who did not. In addition, with the exception of Japan, they also had a higher comorbidity burden and were more likely to have had a prior hip fracture.

Fracture hospitalization rates and length of stay

Rates of fractures requiring hospitalization in the overall DOPPS population did not vary substantively over time (21 per 1000 PY for DOPPS 2 (2002–2004), 25 per 1000 PY for DOPPS 3 (2005–2008), and 24 per 1000 PY for DOPPS 4 (2009–2011); *P*-value for trend = 0.19), and were therefore combined. The incidence of any fracture requiring hospitalization varied across countries ranging from 12 per 1000 PY in Japan to 45 per 1000 PY in Belgium. Hip-specific fracture rates ranged from 3 per 1000 PY (Japan) to 20 per 1000 PY (Sweden) (Figure 1). This burden of fractures in the dialysis population is contrasted with the burden of fractures reported for the general nondialysis population (Figure 2). The rates across all countries included in the DOPPS were substantially higher for patients receiving dialysis as compared with the general population.

The median hospital length of stay varied widely across countries (Figure 3), ranging from 7 days (in the United States; interquartile range = 4–14 days) to 37 days (in Japan; interquartile range = 21–61 days). In Australia/New Zealand, Belgium, Germany, Japan, the United Kingdom, and the United States, overall length of hospital stay was longer for hip fractures than for other fractures ($P < 0.05$).

Postfracture clinical outcomes

The incidence of postfracture clinical outcomes varied across countries (Figure 4). In most countries, mortality rates exceeded 500 per 1000 PY, and when subsequent hospitalizations were also included (composite event), the rates exceeded

Table 1 | Demographics and clinical characteristics of all DOPPS participants, of those who experienced, and those who did not experience a fracture requiring hospitalization, by geographic region

	Europe, Australia, New Zealand			Japan			North America		
	All	Fracture	Nonfracture	All	Fracture	Nonfracture	All	Fracture	Nonfracture
Patients (no.)	18,903	667	18,236	6782	143	6639	9137	324	8813
Hip fractures (no.)	293	293	0	36	36	0	162	162	0
Patient-years	25,858	669	25,189	11,914	157	11,757	10,969	296	10,673
Mean (s.d.), median (IQR), or %									
Age, years (median)	67 (55–76)	74 (65–79)	67 (54–75)	64 (55–72)	68 (60–76)	64 (55–72)	64 (52–74)	71 (59–80)	63 (52–74)
Black (%)	2	1	2	0	0	0	25	13	25
Male (%)	60	43	60	62	46	63	55	47	55
Years on dialysis (median)	1.7 (0.4-4.7)	2.7 (0.8–5.8)	1.7 (0.4-4.7)	3.8 (0.7–9.4)	5.4 (2.2–10.3)	3.8 (0.7–9.3)	1.5 (0.3-4.0)	2.1 (0.6-4.3)	1.5 (0.3-4.0)
Body mass index (kg/m^2)	25 (22–28)	24 (21–28)	25 (22–28)	21 (19–23)	20 (18–22)	21 (19–23)	26 (23–31)	25 (22–31)	26 (23–31)
Diabetes (%)	34	39	33	36	36	36	54	60	54
Hypertension (%)	82	83	82	75	72	75	90	89	91
Coronary artery disease (%)	44	53	44	32	34	32	58	64	58
Congestive heart failure (%)	29	38	29	23	24	23	42	49	42
Cerebrovascular disease (%)	17	23	17	15	17	14	18	23	18
Peripheral vascular disease (%)	30	34	30	16	18	16	32	37	32
Other cardiovascular (%)	36	47	36	30	29	30	33	38	33
Cancer (other than skin) (%)	15	20	15	9	11	9	14	13	14
GI bleeding (%)	5	7	5	5	6	5	7	8	7
Lung disease (%)	13	15	13	3	4	3	18	24	17
Recurrent cellulitis, gangrene (%)	9	13	9	4	5	4	11	13	11
Neurologic disease (%)	11	15	11	9	10	9	13	15	13
Psychiatric disorder (%)	17	21	17	4	4	4	26	25	26
Prior hip fracture (%)	3	12	3	2	8	2	3	9	3
Calcium, total, mg/dl, mean)	9.1 (0.9)	9.2 (0.9)	9.1 (0.9)	8.9 (0.9)	9 (0.9)	8.9 (0.9)	9 (0.8)	9.1 (0.8)	9 (0.8)
Phosphorus, mg/dl, mean)	5.2 (1.8)	4.9 (1.6)	5.3 (1.8)	5.5 (1.5)	5.4 (1.5)	5.5 (1.5)	5.4 (1.8)	5.2 (1.7)	5.4 (1.8)
PTH, intact, pg/ml, mean)	299 (385)	304 (551)	299 (377)	194 (235)	208 (224)	194 (235)	348 (412)	369 (593)	348 (404)
Albumin, g/dl, mean)	3.7 (0.5)	3.6 (0.5)	3.7 (0.5)	3.7 (0.5)	3.7 (0.4)	3.7 (0.5)	3.6 (0.5)	3.5 (0.5)	3.6 (0.5)
Hemoglobin, g/dl, mean)	11.3 (1.6)	11.5 (1.4)	11.3 (1.6)	10.1 (1.4)	10 (1.3)	10.1 (1.4)	11.5 (1.5)	11.5 (1.4)	11.4 (1.5)
Single-pool Kt/V (mean)	1.5 (0.3)	1.6 (0.3)	1.4 (0.3)	1.3 (0.3)	1.4 (0.3)	1.3 (0.3)	1.5 (0.3)	1.6 (0.3)	1.5 (0.3)

Abbreviations: DOPPS, Dialysis Outcomes and Practice Patterns Study; GI, gastrointestinal; IQR, interquartile range; PTH, parathyroid hormone.
Parenthesized values after medians (indicated in first column label) are the interquartile ranges; those after means are the s.d. values.
'All' includes all study participants; 'Fracture' includes only patients who experienced a fracture requiring hospitalization during follow-up.
North America includes United States + Canada; Europe, Australia, New Zealand include Australia, Belgium, France, Germany, Italy, New Zealand, Spain, and Sweden.

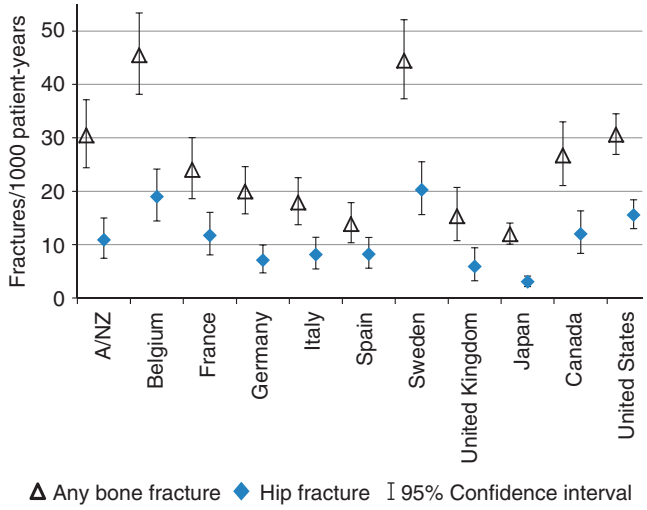

Figure 1 | Incidence of fractures resulting in a hospital admission among participants of the Dialysis Outcomes and Practice Patterns Study (DOPPS), by country. Only the first fracture event for each patient was included in the calculation of these rates. A/NZ, Australia and New Zealand.

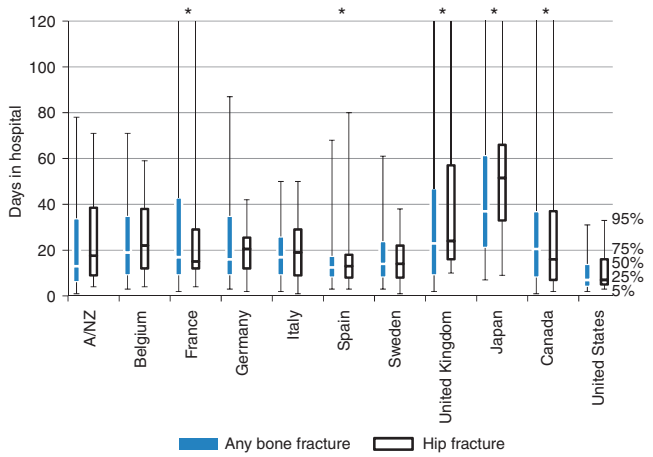

Figure 3 | Length of stay in the hospital for fracture-related admissions, by country. *The numbers of fracture-related hospitalizations with a reported length of stay of >120 days were as follows: Canada—6 any bone fractures and 4 hip fractures; France—4 any and 3 hip; Japan—8 any and 3 hip; Spain—1 any and 1 hip; and United Kingdom—2 any bone fractures and 2 hip fractures. A/NZ, Australia and New Zealand.

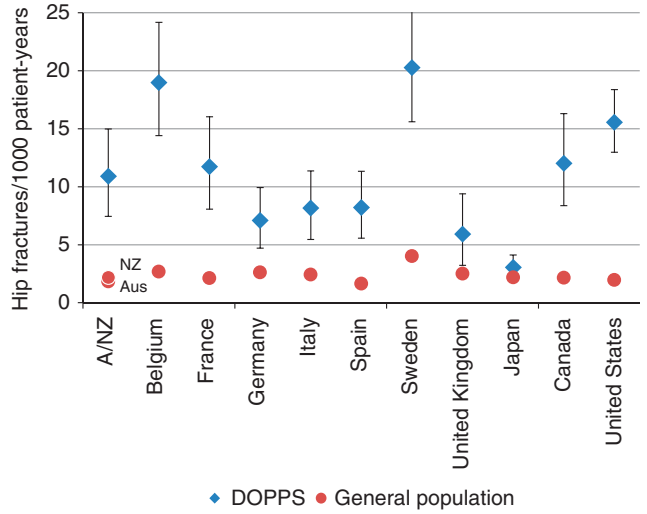

Figure 2 | Hip fracture rates among participants of the Dialysis Outcomes and Practice Patterns Study (DOPPS) and in the general nondialysis population, within each DOPPS country. Rates among DOPPS participants refer to hip fractures requiring a hospital admission; rates in the general population were derived from a review by Kanis *et al.*[14] and may include hip fractures that did not require hospitalization. A/NZ, Australia and New Zealand.

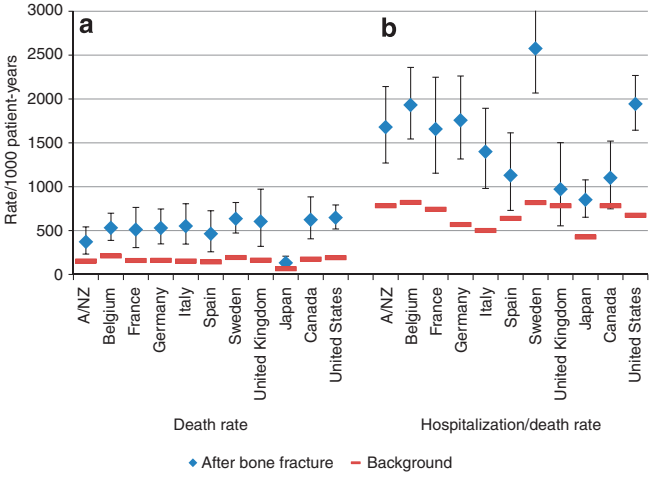

Figure 4 | Death and hospitalization rates in the year following a fracture event requiring hospitalization, by country. (**a**) Death rate. (**b**) Composite death/hospitalization rate. Rates are restricted to events occurring within 1 year of the fracture (fracture admission for death, fracture discharge for hospitalization/death). The background rate is the rate among all participants of the Dialysis Outcomes and Practice Patterns Study (DOPPS), including patients who experienced a fracture and those who did not. A/NZ, Australia and New Zealand.

1500 per 1000 PY. As in the general DOPPS sample, the most common cause of death among patients who experienced a fracture requiring hospitalization was cardiovascular events (45%) and infections (21%). In most countries, unadjusted rates of postfracture clinical outcomes were substantively higher for patients experiencing any type of fracture compared with patients in the general DOPPS hemodialysis sample. Adverse clinical outcomes were also more common for patients experiencing a hip versus other types of fracture, but no statistically significant differences in postfracture outcomes were observed between patients who had a prior history of hip fracture and those who did not (533 vs. 490 deaths per 1000 PY and 1556 vs. 1578 composite death/hospitalization events per 1000 PY). Although women were more likely to experience a fracture, men had a slightly higher mortality rate in the follow-up period. One potential

explanation for this is that women are more likely to die during fracture hospitalization than men, thereby removing women (who may have more severe complications as a result of the fracture) from the cohort that is then followed up for postfracture outcomes.

Survival curves for study participants who experienced and those who did not experience a fracture requiring hospitalization within each DOPPS region are shown in Figure 5a. In each region, the curves separate immediately showing a marked difference between the death rate during the year following the fracture event and the death rate in nonfracture patients. In the fracture group, mortality was highest in the month immediately following the fracture event (Europe/Australia/New Zealand: 87, Japan: 25, and North America: 115 deaths/1000 patient-months), with rates in individual countries 3.8- to 11.6-fold higher in fracture patients compared with the overall DOPPS sample. Mortality rates began to decline in months 1–6 (Europe/Australia/New Zealand: 34, Japan: 6, and North America: 32 deaths/1000 patient-months) and dropped further between months 6 and 12 (Europe/Australia/New Zealand: 18, Japan: 7, and North America: 34 deaths/1000 patient-months). In most countries, mortality rates still remained elevated 1 year after fracture compared with the overall DOPPS sample. Similar patterns were observed for the composite event of death or first hospitalization (Figure 5b).

There were important case-mix differences between patients who experienced a fracture and the general DOPPS population (Table 1), which may also affect the underlying risk of death. We addressed these demographic differences between the two groups using model-based standardization and, despite this, death rates remained substantially elevated among patients who experienced a fracture; this finding was consistent across different patient subgroups (Figure 6). Additional adjustment for comorbidity differences did not materially affect these results (not shown).

DISCUSSION

Our study of over 34,000 patients across 12 countries is the first to quantify health burden related to fractures in an

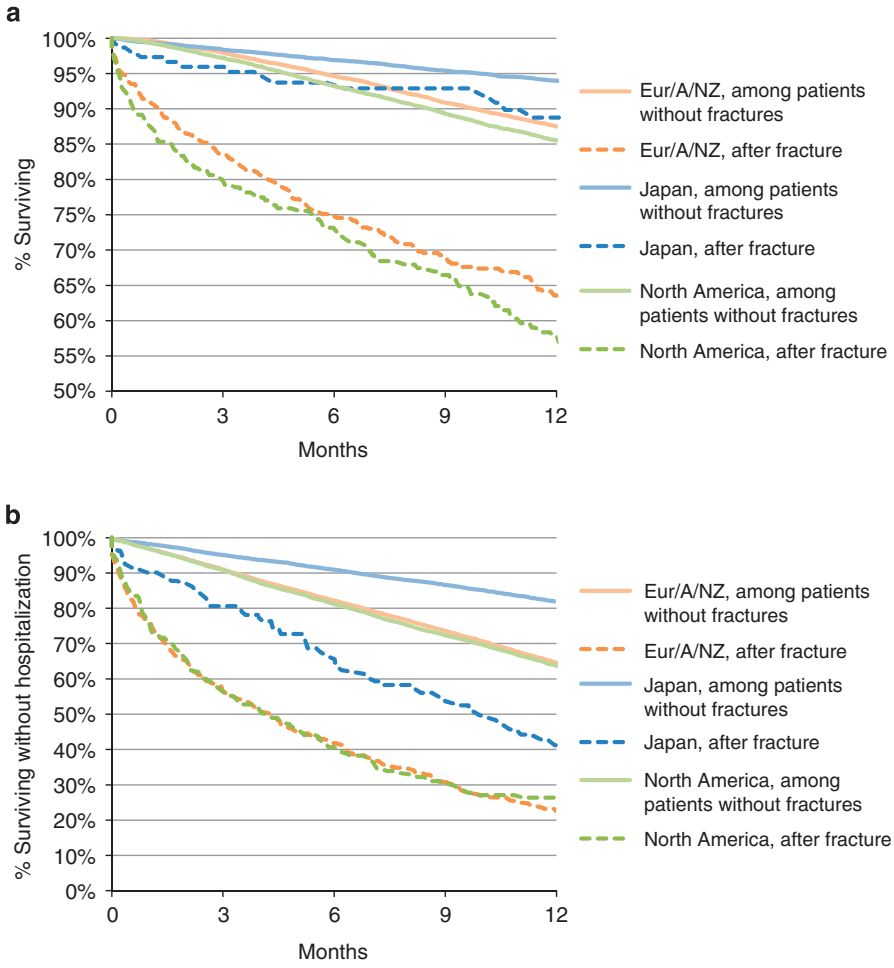

Figure 5 | Time to death and hospitalization among participants of the Dialysis Outcomes and Practice Patterns Study (DOPPS) who experienced and those who did not experience a fracture requiring hospitalization, by DOPPS region. (**a**) Unadjusted survival (time to death) by DOPPS region. (**b**) Unadjusted survival without any hospitalizations (time to first hospitalization or death) by DOPPS region. Eur/A/NZ, Europe, Australia, and New Zealand.

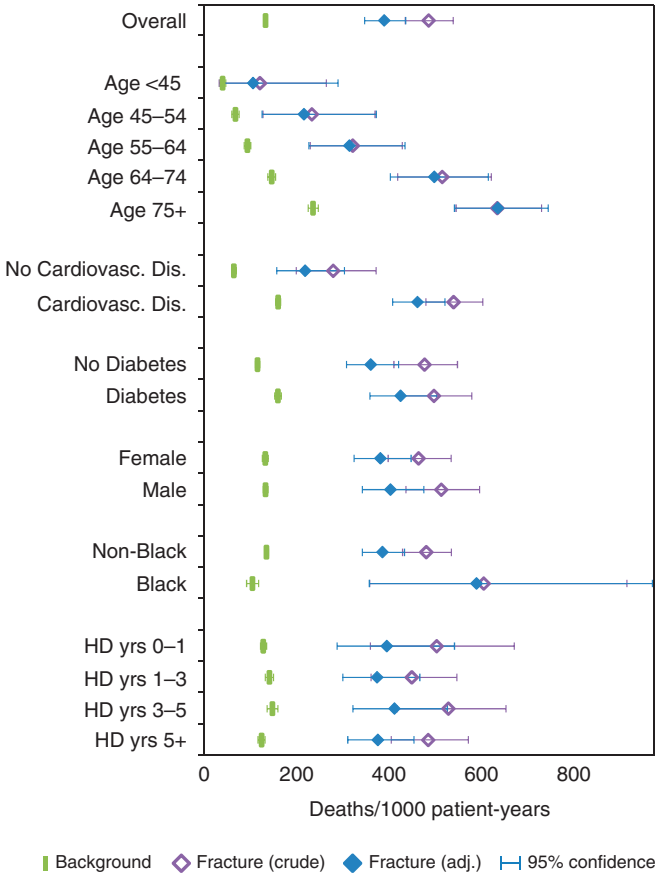

Figure 6 | Mortality rates for fracture versus background patients by strata of patient characteristics. 'Cardiovasc dis' is cardiovascular disease defined as having any of the following conditions: coronary artery disease, congestive heart failure, cerebrovascular disease, peripheral vascular disease, or other cardiovascular disease. 'Adj' is adjusted models, accounting for country, age, DOPPS phase race (Black vs. non-Black), sex, and years (yrs) on dialysis. HD, hemodialysis. Owing to the large sample size of many of the strata, confidence intervals for the overall death rates are very small and therefore not visible in the figure.

international cohort of patients on chronic hemodialysis. In agreement with an earlier report,[3] we found a rate of fracture much higher than that in the general population, with significant variability in fracture rates between countries that could not be explained by case-mix differences. We also report for the first time a markedly elevated rate of subsequent mortality and hospitalization after fracture relative to dialysis patients who did not experience a fracture requiring hospitalization.

Using data spanning 10 years in 12 countries, our study shows considerable variation in the incidence of fractures and postfracture consequences across countries. Overall, country-specific fracture rates were consistent with those reported in a previous study using DOPPS data from 1996 to 2001.[3] The fracture rates across countries observed in this study are consistent with previous studies in dialysis patients,[2,4,5] highlighting fracture as an important clinical outcome in this population. In comparison with the general population, dialysis patients are at a significantly elevated risk of fracture, and this excess risk ranges from 1.5- to 8-fold depending on the country.[4,14] It is important to acknowledge that the comparison of rates from the DOPPS population with the general nondialysis population in this study relied on published fracture rate estimates for the general population in each country,[14] precluding any ability to adjust for case-mix differences (for example, age, gender, race, and so on). These comparisons should be considered in light of this limitation; nonetheless, these data provide evidence describing the potential excess risk of fracture among dialysis patients,[2–5] which is likely attributable to the high prevalence of mineral and bone disorders and other risk factors in the dialysis population. The role of low bone mineral density in the pathogenesis of fractures is not clear;[1,15,16] however, abnormal PTH levels[2,3,8] and the use of psychoactive drugs that may increase the incidence of falls can contribute to an elevated risk of fracture.

Across nearly all countries, fracture events led to long hospital admissions. At one extreme, patients hospitalized in Japan had a median length of stay of ~37 days; at the other extreme, patients hospitalized in the United States had a median length of stay of 7 days. It is quite possible that these differences are largely explained by differences in health-care systems and the delivery of care. In Japan, for example, physical rehabilitation takes place in the hospital as opposed to outpatient care centers (oral communication, Dr Takashi Akiba, 26 May, 2012), and thus prolonged lengths of stay are reasonable. This may also explain why the rate of postfracture clinical outcomes was the lowest in Japan. In a prior DOPPS analysis, dialysis facilities with shorter median hospital length of stay had higher odds of readmission,[17] supporting the hypothesis that hospital admissions that are too short may have a negative effect on subsequent clinical events by precluding the delivery of optimal care.

The clinical burden following a fracture (including mortality and hospitalizations) was substantial and observed across nearly all countries. In the early months following discharge, mortality and hospitalization rates were 2–9 times higher compared with the general dialysis population within each country, standardized on basic demographic characteristics. This finding is consistent with the estimate of a 2.7-fold higher risk reported by Danese *et al.*,[8] using data from the US Renal Data System, and other studies that showed higher mortality rates for patients experiencing a hip fracture.[2,8,13,18] In this analysis, we were unable to distinguish between idiopathic fractures and those potentially attributable to other clinical events that may have occurred concurrently (for example, a stroke resulting in a fall and fracture). Thus, we cannot exclude the possibility that some of the observed excess risk after fracture may be attributable to other events. As patients who experience a fracture tend to have a different clinical profile than those who do not (for example, are older), we compared the risk of mortality and hospitalization after adjusting for demographic differences and found that the rates remained substantially elevated (~3 times higher).

The elevated morbidity and mortality in the early period following a fracture suggests that a bone fracture acts as an 'acute' risk factor for adverse outcomes. Possible contributing mechanisms may include bleeding, prolonged immobilization, malnutrition, and high rates of infections,[19] all of which may precipitate preexisting conditions. These potential risk factors may be directly related to the fracture event or more generally to being hospitalized; it is likely that immobilization and other functional limitations have an important role in increasing frailty and infection risk, and contribute to the high incidence of adverse clinical outcomes.

The fact that morbidity and mortality of fracture patients tended to be higher in the following months up to 1 year after a fracture suggests that additional mechanisms also contribute to adverse outcomes. Several studies have shown higher rates of vascular calcification in the presence of low bone turnover in patients with kidney disease.[20,21] In a cohort of hemodialysis patients, vertebral fractures were associated with vascular calcifications in medium caliber arteries.[22] In the general population, decline in bone mineral density was associated with progression of aortic calcifications.[23,24] Altogether, these findings indicate that dysregulation in bone metabolism is likely to affect calcium deposition in arteries and may contribute to the pathogenesis of cardiovascular disease in this population. However, detailed pathogenic mechanisms remain to be clarified.

In the general population, serious fractures are associated with high health-care costs, with the estimated cost for hip fracture in the United States exceeding $20 billion per year.[25] High costs related to fractures have also been reported among US dialysis patients.[8] Although data available within the DOPPS preclude formal cost studies, the long length of hospital stay and high readmission following fracture events indicate that fractures in hemodialysis patients are associated with high resource utilization. Future studies should investigate the postfracture health-care resource utilization to more fully quantify their burden.

Given the high health and economic burden related to bone fractures, strategies for fracture prevention should be identified and implemented.[26] Interventions will most likely target both abnormalities in bone structure and other modifiable risk factors peculiar to the hemodialysis population, with particular attention paid to subgroups of patients who are at higher risk of fractures (for example, elderly, women, longer duration of end-stage renal disease). It is possible that high PTH levels may further increase the risk of fracture in this population.[3,8] Given the association between high PTH and cardiovascular outcomes,[18] most clinicians prescribe a therapeutic regimen aimed at lowering PTH levels. However, both high and low PTH levels have been associated with fracture rates.[2,3,8] Whether maintaining PTH levels within guideline targets will affect fracture risk remains to be demonstrated. This is particularly important given the recent trends toward higher PTH levels reported in most DOPPS countries, with ~18% of US participants in December 2011 having PTH >600 pg/ml.[27,28] Other strategies aimed at fracture prevention will include identification of frail patients who may have an increased risk of falls,[26] physical therapy, as well as avoidance of hypotensive episodes, and careful prescription of psychoactive medications that may contribute to reducing fall-related fractures.[3,26] Vitamin D supplementation resulting in normalization of serum 25-hydroxy vitamin D levels may reduce the risk of falls, as demonstrated in older individuals without known kidney disease.[29] Finally, given the strong association between malnutrition, low body weight, and bone health, nutritional interventions aimed at improving the nutritional status of patients and maintaining healthy body weights may affect the risk of bone fractures.

The extensive DOPPS database and detailed data collection allowed us to report the rates of other major bone fractures and not only limited to hip fractures, as done by most prior studies;[4,5,13] however, details on other fracture types were not available. Additional limitations of this analysis are related to the observational nature of the DOPPS. First, as we only studied fractures resulting in hospitalizations, our findings likely underestimate the total incidence of fractures in hemodialysis patients. Second—although unlikely—we cannot exclude that differences in reporting hospitalization data may have contributed to the observed variability in fracture rates across DOPPS countries. Third, once patients are transferred out of the DOPPS facility, information on patient care is no longer captured. In some countries, discharge to long-term care or rehabilitation facilities is the standard of care and may represent additional burden and significant resource utilization not characterized in our analysis. Finally, data on surgical and/or rehabilitation approaches to management of serious fractures were not collected, and therefore the effect could not be examined in this investigation.

In conclusion, using the international DOPPS cohort, we demonstrate that bone fractures are relatively common among hemodialysis patients in many countries and pose a significant health burden. Additional studies are needed to further quantify the overall burden related to fractures and to identify modifiable practices that may help minimize the fracture risk in this frail population.

MATERIALS AND METHODS

Data source

The DOPPS is a prospective cohort study of in-center hemodialysis patients ⩾18 years old in 12 countries (Australia, Belgium, Canada, France, Germany, Italy, Japan, New Zealand, Sweden, Spain, the United Kingdom, and the United States). The DOPPS study design has been described previously.[30,31] Briefly, the study population comprises randomly selected patients from a random sample of dialysis facilities within each country. Detailed demographic, comorbidity, and laboratory data were collected at study entry and updated throughout follow-up. Information on hospitalization and mortality (with primary and secondary causes) and reasons for loss to follow-up were also collected. In each DOPPS phase, patients lost to follow-up were replaced in order to maintain a representative cohort within each country. Although many DOPPS facilities and some study participants in a given phase continued participation

into a subsequent study phase, there was no overlap of the follow-up periods analytically. Informed patient consent was obtained in accordance with local requirements.

Study population

This study included all study participants in DOPPS phase 2 (2002–2004), phase 3 (2005–2008), and phase 4 (2009–2011).

Outcomes

We identified all first hospitalizations (defined by an overnight hospital stay) with an associated fracture diagnosis code. In the DOPPS data set, fractures were coded as either 'hip' or 'other'; information on other types of fractures (for example, vertebral fractures) were not available. Therefore, we characterized fracture-related hospitalization as either 'any fracture' or 'hip fracture.' We defined the length of stay in the hospital as the time between admission and either date of discharge or, if the patient died in the hospital, date of death. Length of stay was combined for overlapping hospitalizations or for hospitalizations occurring within 5 days of each other, where subsequent hospitalization(s) appeared to be a continuation of the first admission (for example, physical therapy following the fracture event). For fracture event rates, follow-up started at study enrollment and continued until the first of death, fracture hospitalization, transplantation, renal replacement therapy modality switch, recovery of renal function, departure from the facility, or end of follow-up.

For the postfracture outcomes, we identified all hospitalizations and deaths over the period of 1 year after discharge from the fracture hospitalization. For analyses of postfracture mortality alone, follow-up started on the fracture admission date. For analyses of the composite event, follow-up started upon discharge from the hospital and continued until the first of death, subsequent hospitalization, transplantation, renal replacement therapy modality switch, recovery of renal function, departure from the facility, or 365 days.

Statistical analysis

Standard descriptive statistics for categorical variables (count (n), percentage (%)) and continuous variables (mean, s.d., median, 25th/75th percentile) were used to characterize patients at study enrollment, by DOPPS region (North America = United States + Canada; Eur/ANZ = European countries + Australia and New Zealand; and Japan) and for patients who experienced a fracture-related hospitalization during follow-up.

Fracture rates. Incidence rates and 95% confidence intervals were estimated by country for fractures of any type and fractures of the hip requiring hospitalization by country. Rates were calculated as the total number of events divided by the patient time accumulated before censoring. The 95% confidence intervals for rates were estimated using Byar's approximation to the Poisson distribution.[32] The median, 5th, 25th, 75th, and 95th percentile estimates for the fracture hospitalization length of stay were also calculated.

Postfracture events. All-cause mortality rates and associated 95% confidence intervals were estimated for 1 year after discharge from the fracture hospitalization. Rates were also calculated for a composite event of death or first rehospitalization in an effort to minimize the effect of death as a competing event.

Comparison of the postfracture events with a reference population. To provide some context to gauge the clinical significance of fracture consequences, rates of death, starting at the initial admission, and the composite of death and first hospitalization, starting at discharge, were estimated for the overall DOPPS population within each country. Then, the postfracture population was standardized to the age, sex, race, and length of time on dialysis distribution in the overall population within each country, so that standardized events could be estimated.

DISCLOSURE

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DISCLAIMER

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Diabetes and Digestive and Kidney Diseases or the National Institutes of Health.

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